Isomorphism between morphological and functional graphs of the cell and classification of cells by the extensions of graphs

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Morphological and functional graphs of the cell are constructed, expressing dynamic ontogenetic transformations between six different types of membranes of organelles and the interrelations between six different functions of vital significance for the cell. Morphisms (epimorphisms) from different biological graphs to a functional graph are constructed. It is shown that there exists an isomorphism between morphological and functional graphs which expresses the most essential forms of vital processes. It is further shown that the components with vital functions transform and transfer to each other. To classify and construct cell structures the apparatus for extensions of graphs developed by the author is used, which enables hierarchical biological systems to be described.

Keywords: theoretical biology

The present work concerns an attempt to express some basic phenomena occuring in a cell by means of graphs. N. Rashevsky [1, 2] suggested the construction of an oriented graph for every organism. The graphs corresponding to different organisms are formed from each other with the help of the general rule of geometrical transformation and can be mapped onto each other epimorphously preserving some basic relations.

To some extent our work is close to Rashevsky's works. We shall try to construct functional and morphological (referring to ontogenetic mutually transformed membranes of organelles) graphs of the cell. We wish to prove that between functional and morphological graphs there is isomorphism expressing the most essential features of vital processes. In the future, similar graphs will make it possible to consider the organization of biological processes in a cell in a different way, to find those forms of order which are not revealed at the present stage. It is natural to try to apply different constructions of the theory of graphs to construct biological structures (see [3] for an example where the apparatus of the extension of graphs is used).

Consider a graph G viewed intuitively as an encoding of a system consisting of objects labelled v and various interrelations between them labeled i.

Being a graph implies that V_G the set of its vertices, and I_G, the set of its arrows, are given. Moreover each arrow from I_G has a source and a target from V_G. In other words G is determined by two sets V_G, I_G and two mappings from I_G to V_G,

$$\text{`}source\text{'}, \text{`}target\text{'} : I_G \to V_G$$

such that any arrows having the same source and the same target are the same.

Furthermore let $(G_v)_{v\in V_G}$ be a family of graphs, one for each vertex of G.

An extension of the graph G, with the family $(G_v)_{v\in V_G}$ is a graph H together with an epimorphism $\sigma: H\to G$ (epimorphism $\sigma: V_H \to V_G$ such that images of incident vertices are either incident or equal), such that $\sigma^{-1}(v)\approx G_v$ for each $v\in V_G$. An extension (H,σ) and family of epimorphisms $\sigma^{-1}(v)\to G_v$ determines a certain partial morphism:

$$f:(\coprod_{v\in V_G} V_{G_v})\times I_G \to \coprod_{v\in V_G} 2^{V_{G_{v'}}} \qquad (1)$$

such that $f(v^\alpha,i)\in 2^{V_{G_{v'}}}$, where: $i\in I_G$, $v^\alpha\in V_{G_v}$, $\alpha=1,...,n$; v^α is a source of the arrow i and v' is the target of the arrow i, n is the number of vertices in $f^{-1}(v)$.

To make the notion of graph extension more understandable, let us turn to a particular example: consider the graph G in fig.1a, whose vertices represent two objects v_1 and v_2 and two interrelations, labelled, respectively, i_1 and i_2, incidence for i_1 being from v_1 to v_2 and that for i_2 being

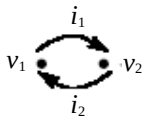

Figure 1 a. Graph G.

from v_2 to v_1. That is, i_1 begins in v_1 and ends in v_2, and i_2 begins in v_2 and ends in v_1.

We next turn to the definition of a morphism between graphs, say, a morphism from a graph G_{v_1} (fig. 1b) to a graph G_{v_2} (fig. 1c). Let us assign to the vertex v_1^1 of the graph G_{v_1} the vertex v_2^1 of the graph G_{v_2}: $v_1^1 \to v_2^1$.
In general, a morphism f of graphs $G_1\to G_2$ is a mapping $f: V_{G_1}\to V_{G_2}$ such that if there is an arrow with source v and target v', then either $f(v)=f(v')$ or there is an arrow with source $f(v)$ and target $f(v')$.

If the vertex v_2^2 of the graph G_{v_2} is assigned to the vertex v_1^2 of the graph G_{v_1}, then the arrow i_2^1 corresponds to the arrow i_1^1. Hence we obtain a morphism of graphs f with

$$f(v_1^1) = v_2^1,\ f(v_1^2) = v_2^2.$$

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Now what is the definition of an epimorphism from a graph G_1 to the graph G_2. Intuitively, this means that each vertex of G_2 is the image of some vertex from G_1.

The map f above is an example of a map which is not an epimorphism, since the vertex v_2^3 and the arrows i_2^3, i_2^2 have empty inverse images under f.

On the other hand, define another map g from the graph G_{v_2} to the graph G_{v_1} by $v_2^1 \to v_1^1$, i.e. by assigning to the vertex v_2^1 the vertex v_1^1, and furthermore $v_2^3 \to v_1^1$, $v_2^2 \to v_1^2$; one can check easily that this is a graph morphism which is an epimorphism (see figs 1b and 1c).

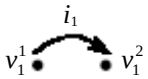

Figure 1 b. Graph G_{v_1}.

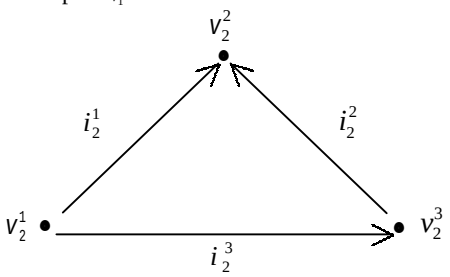

Figure 1 c. Graph G_{v_2}.

Let us now define an extension of a graph G by a family G_v of graphs. For simplicity let us assume that the family $\{G_v\}_{v\in V_G}$ consists of two graphs G_{v_1} and G_{v_2}. Then, construct a graph H as follows: place at each vertex of G the corresponding graph from the family, i.e. in our case place at the vertex v_1 the graph G_{v_1} and at v_2 the graph G_{v_2}. Then construct the new arrow h starting at some vertex of $G_{v_1}$and ending in G_{v_2} and starting at some vertex G_{v_2} and ending in G_{v_1}(see Fig. 1d).

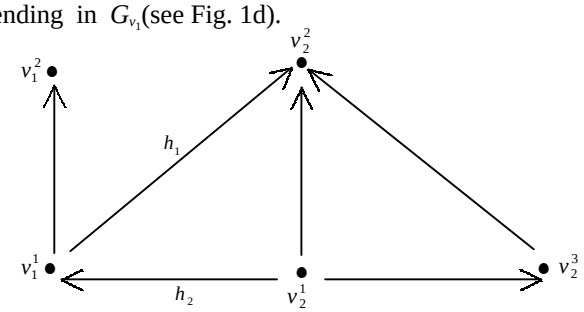

Figure 1 d. Graph H.

Let us show that there is an epimorphism from H to G. Indeed, define the map σ by $\sigma(G_{v_1}) = v_1$, $\sigma(G_{v_2}) = v_2$ and $\sigma(h_1) = i_1$, $\sigma(h_2) = i_2$, then clearly σ is such an epimorphism.

In the language of system theory, H is a compound system consisting of two subsystems G_{v_1} and G_{v_2}, interrelated via h_1 and h_2, whereas considered as units, they are interrelated via the arrow i_1. The arrow i_1 encodes in itself multiple interrelations, in our particular example two interrelations h_1 and h_2. In principle this is a mathematical description of the concept of decomposing a whole into interrelated parts.

Such extensions are naturally realized in the following way: as G we take the graph G_{ee} corresponding to the relation of exocytosis and endocytosis of the cell (fig. 2a) and with the corresponding G_{ex}, G_{en} (figs 2b and 2c) and f

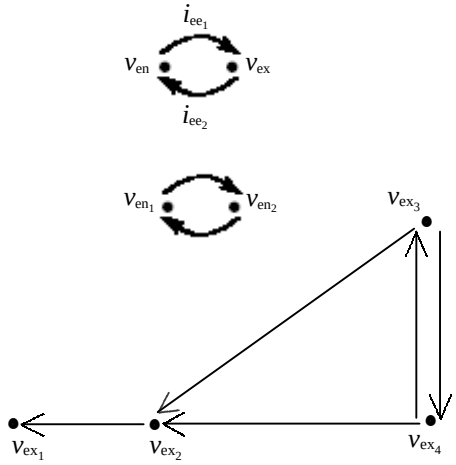

Figure 2. From top to bottom:
a) the graph G_{ee} corresponding to the relation of exocytosis and endocytosis of the cell;
b) the graph G_{en} expressing endocytosis of the cell;
c) the graph G_{ex} expressing exocytosis of the cell.

we get as an extension graph G_f of the cell itself, the graph of ontogenetic mutual transformations of the membranes of organelles G_{mem}, i.e. graph A in our earlier work [4]. We can say that instead of vertices expressing endocytosis and exocytosis in the graph G_{ee} we substitute their corresponding graphs G_{ex} and G_{en} and construct new arrows, the sources of which will be some vertices $v\in G_{ex}$ or $v\in G_{en}$ and the targets will be some vertices $v\in G_{ex}$ or $v\in G_{en}$. In its turn graph G_{mem}, i.e. graph G_f can also be extended if we know the corresponding graphs for each membrane. It should be noted that the graph which is being extended is hierarchically at a higher level than the graph obtained after extension, i.e. if some graph expresses relations between different components at some level, then after its extension we get the graph expressing relations between the subcomponents of these components at a lower lewel. Thus, different cellular types are characterized by mappings of the extension f, i.e. the cells are marked and coded with different mappings of the extension. Of course not all graphs G_f constructed by different f will correspond to cells. For example, with some f's such graphs G_f are obtained which are trees: and there are 1540944 non-isomorphic oriented 6-vertex graphs altogether (6 - orgraphs) [5]. From this number 6 trees and 1296 marked trees must be subtracted. The same could be said about simple orgraphs. After extension of graph G_{ee} by graphs G_{ex} and G_{en} and the two mappings f and g, the extended graphs G_f and G_g may happen to be isomorphic. The isomorphism between G_f and G_g, i.e. the equivalence between mappings, is tested in the following way:

$$g[T(v),i]=T[f(v,i)], \qquad (2)$$

where $i\in I_G$,$v\in V_{G_v}$, and T is the automorphism of the family $(G_v)_{v\in V_G}$.

Let us illustrate the above by an example. Let the graph G_{ee} be given (fig. 2a). Let also graphs G_{en} and G_{ex} be given (fig. 2b and 2c). Let the mappings of extension f and g be given, defined in the following way:

$f(v_{en_1}, i_{ee_1})=\{v_{ex_1}\}$; $g(v_{en_2}, i_{ee_1})=\{v_{ex_1}\}$

$f(v_{ex_1}, i_{ee_2})=\{v_{en_2}\}$; $g(v_{ex_1}, i_{ee_2})=\{v_{en_1}\}$

Let us construct the extensions G_f and G_g of the graph G_{ee} by graphs G_{en} and G_{ex} and the mappings f and g. If we apply the equality (2) then G_f and G_g will be isomorphic (fig. 3).

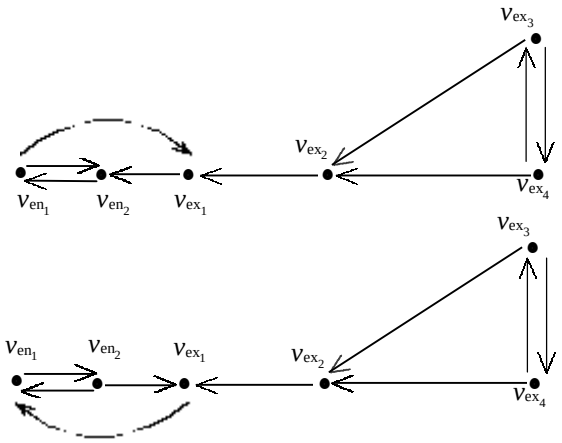

Figure 3. Isomorphism between the graphs G_f (upper) and G_g (lower).

Thus, after extension of the graph G_{ee} by graphs G_{en} and G_{ex} and the equivalent mappings of f and g we obtain isomorphic graphs G_f and G_g representing the same cell. Now our primary task is the construction of graph A, i.e. graph G_{mem}, as described in the next section.

Construction of the graph of ontogenetic transformations of membranes of organelles - the morphological graph A (the graph G_{mem})

In modelling a cell (as well as in modelling any system) it is necessary to define the most essential features, and this may be done with a block-scheme. From common theoretical, mathematical, cybernetical etc. considerations we have described such a block-scheme [4],[6-8].

We assume that in a cell there is a such a dynamical composition which covers the relations between membranes and expresses the functional morphology of the cell. Many biological processes occurring in the cell rest upon this composition as the basis. The relations between various membranes can be expressed by a graph showing the dynamics of morphological transformations in ontogenesis [4],[6-8]. This graph is the morphological block-scheme of the cell (fig.4). The vertices of graph A denote membranes and the arrows denote mutual transformations of membranes in ontogenesis. These arrows are constructed on the basis of data from different authors; for example, refs [9-13]were used to construct the arrow from the Golgi complex to the plasmalemma. For the non-biologist reader we'll try to make more explicit the membranes, their intertransformations and biogenesis. Biological membranes are lipid-protein complexes in which the lipid molecules form an ordered (liquid-crystallic) layer, in which the protein molecules are inserted. Topologically, membrane surfaces are closed two-dimensional oriented (two-sided) surfaces. The two sides (inner and outer) bounding this layer differ from each other significantly. Discontinuities of biological membranes, with the formation of free boundaries, vanish practically instantaneously by "annealing", with recovering of continuity of the membrane surface. The surface of each cell is covered by the plasma (outer) membrane. For the simplest cells (prokaryota) this is the only membrane system. Topologically, it is a sphere surface.

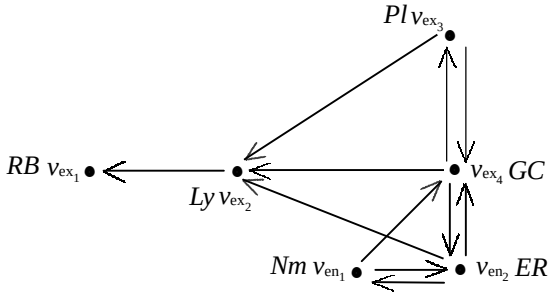

Figure 4. The morphological graph A (graph G_{mem} of ontogenetic intertransformations of membranes of organelles. *RB* is the residual body, *Ly* the lysosome, *Pl* the plasmalemma (plasma membrane), *GC* the Golgi complex, *ER* the endoplasmic reticulum, and *Nm* the nuclear membrane.

In cells of higher type (eukaryota) the inner cell membrane systems are very variable both morphologically and functionally. The membrane systems of eukaryotic cells are closed surfaces (membranic organoids) of various topological genus, which are embedded into the closed surfaces formed by the plasma membranes, i.e. into spheres. Moreover, most of the vital processes of a cell are related to membranes. In order to understand the morphofunctional organization of the cell, consideration of the dynamics of membrane transformations—topological transformations of surfaces formed by membranes—is most important.

Among the most complicated of these systems is the outer membrane of the nucleus, which is topologically a sphere, i.e. a sphere embedded into another one. The outer membrane of the nucleus consists of membrane surfaces of two types, which are related to each other by channels (holes piercing the membrane). Since the number of holes is very high, the genus of the surface of the nucleus is very high too. Moreover the number of holes varies according to various functional activities.

Bubbles (small spheres), or fragments with holes, continuously separate from the outer nuclear surface. Furthermore, these small bubbles form, by coalescence, surfaces of other types, in particular the endoplasmic reticulum. Hence, topological transformations of the nuclear membrane take place continuously—both its genus and connectivity changes.

Topologically, membrane circulation is the process of change of membrane connectivity—i.e. when some parts

become cut out and the cutouts closed up by spheres, and simultaneously free boundaries of membranes become glued in. In their turn, small membrane spheres again coalesce with each other and newly formed bubbles become inserted in the membrane of the plasmalemma. Thus the bubbles separated from the Golgi complex form the plasmalemma, i.e. a membrane surface of one type (the Golgi surface) forms a membrane surface of another type (the plasmalemma).

Similar facts hold concerning the interrelations of pairs of other membrane surfaces. Their topological differences determine functional differences, whereas topological intertransformations relate the functionalities of membrane-based organelles of different types, and the possibility of their realization is a necessary condition for the functioning of the synthetic and transportational succession of the cell.

The construction of the functional graph D

Functions of vital importance take place in the cell: the reception (assimilation) of food and energy, the decomposition and synthesis of new substances, and their storage and excretion. In the work [4] the list of functions did not include the transport of nuclear metabolites; it is now included. These functions are interrelated in such a way that they form the administrative contour of the cell. To support life as a whole it is necessary to have the complete set of vital functions. Failure to perform even only one of them is incompatible with life. The set of these six functions is the same for all organisms.

A priori the interrelation of vital functions in similar systems can be expressed by the functional graph *D* (fig. 5).

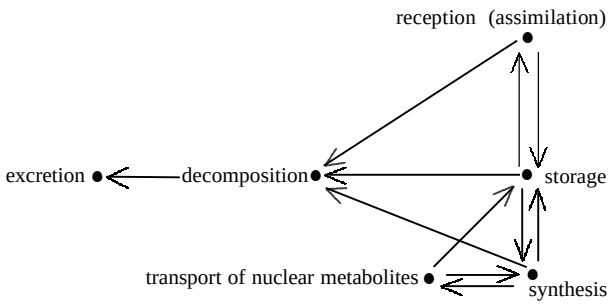

Figure 5. The functional graph *D*.

Functional graphs have also been constructed by other authors. Graph *D* is the functional block cheme of the cell. In the work [8] it is shown that there is morphism from the biological graph of Rashevsky [1], [2] and from other graphs onto the functional graph *D*. Thus it follows that graph *D*, although given in simplified form, has well-grounded validity.

Isomorphism between the morphological graph A and the functional graph D

We shall now show that there is isomorphism between the graphs *A* and *D*. It will be natural if we construct a morphism between *A* and *D* in the following way: we shall attribute the plasma membrane component of graph *A* to the function of "assimilation"of graph *D*, the lysosome to the function of "decomposition", the Golgi complex to "storage", the endoplasmic reticulum to "synthesis", the residual body to "excretion", and the nuclear membrane to "transport of nuclear metabolites". In other words, we correlate the functions performed by these membranes in the cell with the different types of membranes. The morphism constructed between the graphs *A* and *D* in such a way is isomorphism.

Thus, the directions of morphological and functional relations coincide with each other. Isomorphism between the functional graph *D* (the functional block-scheme) and the morphological graph *A* (the morphological block-scheme) is an important fact, it accounts for the essence of circulation in the cell. Reconstructions of membranes, when their connectedness and the genus of the surface change, constitute the necessary conditions for the "administrative" control of the cell.

It is most probable that the cell differs from non-biological systems in this point, that the components performing the vital functions transform into one other.

In our earlier work [4] we raised the question whether the circulation of membranes as the graph *A* is the structural expression of the the functional graph *D*, i.e. the graph of vital functions, and one of the most specific signs for the biology of the cell, and indeed life in general.

Now we can give a positive answer to this question. The six mutually related functions performed by those membranes which are reconstructed in ontogenesis are the cause, i.e. the mechanism, of the reconstruction.v_{ex_1}

It can be shown that the graph *A* is the extension G_f of the graph G_{ee} by G_{en} and G_{ex} and the mapping

$$f:(\coprod_{v\in V_G} V_{G_v})\times I_G \to \coprod_{v\in V_G} 2^{V_{G_{V'}}}$$

defined in the following way:

$f(v_{en_1}, i_{ee_1})=\{v_{ex_4}\}$; $f(v_{en_2}, i_{ee_1})=\{v_{ex_2}, v_{ex_4}\}$; $f(v_{ex_4}, i_{ee_2})=\{v_{en_2}\}$,

where v_{en_1} is the nuclear membrane, v_{en_2} is the endoplasmic reticulum, v_{ex_1} is the residual body, v_{ex_2} is the lysosome, v_{ex_3} is the plasmalemma, v_{ex_4} is the Golgi complex. Ontogenetic intertransformations of the membranes of the cell are characterized by this mapping f (fig. 4).

If the second mapping g is also given and if G_f and G_g are the graphs of the cell, then with the help of the equality (2) we can predict whether the graphs G_f and G_g will be the graphs of the same cell, or of different cells.

Finally we can note that construction of a graph of a complex biological organism from a simple (primordial) graph in Rashevsky's work is virtually an extension too, although in his works the word extension is never mentioned [1, 2].

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